

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY


(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D U 8 JUL 2005

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Applicant's or agent's file reference RD-ATC-32		FOR FURTHER ACTION See Form PCT/PEA/416	
International application No. PCT/GB2004/002583	International filing date (day/month/year) 17.06.2004	Priority date (day/month/year) 17.06.2003	
International Patent Classification (IPC) or national classification and IPC A01H5/00, C12N15/82, C12N15/29, C07K14/415, A23L1/0522			
Applicant ADVANCED TECHNOLOGIES (CAMBRIDGE) LIMITED et al.			
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>			
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input checked="" type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the International application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>			
Date of submission of the demand 12.01.2005		Date of completion of this report 07.07.2005	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer Loubradou, G Telephone No. +49 89 2399- 8543	

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**INTERNATIONAL PRELIMINARY REPORT
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International application No.
PCT/GB2004/002583

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language, which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

Description, Pages

1-55 as originally filed

Sequence listings part of the description, Pages

1-13 as originally filed

Claims, Numbers

1-54 as originally filed

Drawings, Sheets

1/7-7/7 as originally filed

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-18, 20, 22, 24, 27-54
	No: Claims	19, 21, 23, 25, 26
Inventive step (IS)	Yes: Claims	
	No: Claims	1-54
Industrial applicability (IA)	Yes: Claims	1-54
	No: Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and /or

2. Non-written disclosures (Rule 70.9)

see separate sheet

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Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:
 - a. type of material:
 - ☒ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☒ in written format
 - ☒ in computer readable form
 - c. time of filing/furnishing:
 - ☒ contained in the international application as filed
 - ☒ filed together with the international application in computer readable form
 - ☐ furnished subsequently to this Authority for the purposes of search and/or examination
 - ☐ received by this Authority as an amendment on
2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
3. Additional observations, if necessary:

**INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(SEPARATE SHEET)**

International application No.

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Reference is made to the following documents:

- D1: LAZARO A ET AL: "SIGNAL PEPTIDE HOMOLOGY BETWEEN THE SWEET PROTEIN THAUMATIN II AND UNRELATED CEREAL ALPHA AMYLASE-TRYPSIN INHIBITORS" FEBS LETTERS, vol. 239, no. 1, 1988, pages 147-150, XP002297306 ISSN: 0014-5793
- D2: MACGREGOR E A ET AL: "Structural models of limit dextrinase inhibitors from barley" JOURNAL OF CEREAL SCIENCE, vol. 31, no. 1, January 2000 (2000-01), pages 79-90, XP002297305 ISSN: 0733-5210
- D3: DINGES JASON R ET AL: "Mutational analysis of the pullulanase-type debranching enzyme of maize indicates multiple functions in starch metabolism." PLANT CELL, vol. 15, no. 3, March 2003 (2003-03), pages 666-680, XP002297307 ISSN: 1040-4651
- D4: SLATTERY C J ET AL: "Engineering starch for increased quantity and quality" TRENDS IN PLANT SCIENCE, ELSEVIER SCIENCE, OXFORD, GB, vol. 5, no. 7, July 2000 (2000-07), pages 291-298, XP002241850 ISSN: 1360-1385
- D5: WO 98/50562 A (DU PONT ; BROGLIE KAREN E (US)) 12 November 1998 (1998-11-12)

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- 1- D1 discloses the nucleotide and polypeptide sequence of the limit dextrinase inhibitor from barley (see Figure 1 of D1). The polypeptide sequence of D1 differs at 2 positions from the sequence of SEQ ID N°2 of the present application (98,6% of identity) and the nucleotide sequence of D1 shares 99% identity with the sequence of SEQ ID N°1 of the present application. The polynucleotide of D1 is inherently cloned in a vector having a selectable marker gene.
Therefore, claims 19 and 21, 23, 25 and 26 are not novel (Article 33.2 PCT).
- 2- D2 discloses the sequences of the low and high pl inhibitors from barley (Figure 1 of D2). Said sequences are comprised in the sequence of SEQ ID N°2.
Therefore, claim 22 is not novel (Article 33.2 PCT).
In addition, the disclosure of the sequence of a polypeptide is inherently a

disclosure of the sequence of the polynucleotide encoding said polypeptide. As a consequence, said polynucleotide cannot involve an inventive step.

Therefore, claim 20 does not involve an inventive step (Article 33.3 PCT).

3- The subject-matter of claims 24, 27, 28 and 29 is immediately derivable from the subject-matter of D1 or D2 and therefore cannot involve an inventive step (Article 33.3 PCT).

4.1 The polypeptides of D1 and D2 are clearly identified in D2 as limit dextrinase inhibitors (see D2, the abstract and page 88 right-hand column last paragraph). D2 further indicates that the inhibitors are important for the malting and brewing industries (page 80 left-hand column, lines 17 to 23) and that a reduction in the activity of said inhibitors should lead to a greater fermentability.

Therefore, there is a motivation in the art to generate plants having a reduced level of limit dextrinase inhibitor activity. An obvious solution is to generate transgenic plant wherein the expression of the limit dextrinase inhibitor is down regulated, for example by using the anti-sense technology.

In addition, it can be noted that the plants obtained by the method of claims 1-18 are not different from plants transformed with an anti-sense construct down-regulating the expression of the barley limit dextrinase inhibitor.

Therefore, claims 30 to 33 and 42 to 46 do not involve an inventive step (Article 33.3 PCT).

4.2 The applicant is also invited to note that there is a general motivation in the art to alter/understand starch metabolism in plants and that one of the target is limit dextrinase (pullulanase) (see for example: D3, the abstract; D4 the abstract, page 294 right-hand column the last paragraph and page 296 left-hand column, the paragraph entitled "Starch debranching enzymes"; D5 page 1 lines 17 to 22 and lines 37 to 39). It is obvious for the skilled person that modifying the expression of the limit dextrinase inhibitor (overexpression or down regulation) will result in modifications in the limit dextrinase activity. Therefore, plants overexpressing the limit dextrinase inhibitor are also considered as lacking an inventive step.

The plants of claims 34 to 41 are apparently **inherently** obtained following either down regulation or overexpression of the limit dextrinase inhibitor, therefore said plants cannot involve an inventive step (Article 33.3 PCT).

The objection applies *mutatis mutandis* to the starch of claims 48 to 54.

5. It is obvious for the skilled person facing the problem of obtaining a plant having an altered ability to degrade starch that any modification of a gene involved in starch degradation will solve the problem. It is well known in the art that limit dextrinase is involved in starch degradation and that the limit dextrinase inhibitor regulates the activity of limit dextrinase (see for example D2 and D3). Therefore, the solution consisting in altering the expression of the limit dextrinase inhibitor in order to modify the activity of limit dextrinase is considered obvious. Therefore, claim 3 does not involve an inventive activity (Article 33.3 PCT). Dependent claims 4 to 18 do not appear to contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step.
6. The attention of the applicant is drawn to the fact that the modification mentioned in claims 1 and 2 are not limited to the specific starch granules modifications observed in the examples but are drafted in a very broad way. The following objection is based on this fact.
The method of claim 1 is not directed to a specific modification of the starch granule and the method of claim 2 defines de modification so broadly that they cover most of the possible modifications.
Facing the problem of modifying starch granules in general, it is obvious for the skilled person that modifying the activity of any gene involved in starch metabolism would be suitable. The barley limit dextrinase inhibitor is known to regulate the activity of the limit dextrinase which plays an important role both in starch synthesis and starch degradation. Therefore, It is obvious for the skilled person that modifying the expression of the limit dextrinase inhibitor will lead to starch granule modification *via* the inhibition or lack of inhibition of the limit dextrinase. Therefore, claims 1 and 2 are not considered to involve an inventive activity (Article 33.3 PCT).
7. Claims 1 to 54 meet the requirements of Article 33.4 PCT.

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